hereby certify that this with the United States 1 Office to Addressee" service w indicated above and is address and Trademarks, Washington, D.C. 20231.

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Attorney Docket 248432800200

THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: U.S. Patent 4,844,882

Issued: July 4, 1989

To:

Widder et al.

For:

CONCENTRATED STABILIZED

MICROBUBBLE-TYPE ULTRASONIC

IMAGING AGENT

TRANSMITTAL LETTER

The Honorable Commissioner of Patents and Trademarks **Box Patent Extension** Washington, D.C. 20231

Sir:

Enclosed are the following:

- Application for Extension of Patent Term Under 35 U.S.C. Section 156.
- A Certified Duplicate Application for Extension of Patent Term Under 2.

35 U.S.C. Section 156.

- Three (3) Working Copies of Application for Extension of Patent Term Under 35 U.S.C. Section 156.
 - A check in the amount of \$1,000.00.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any

090 FT 09/27/94 4844882

required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to our Deposit Account No. 03-1952.

Respectfully submitted,

Freddie K Park

Registration No. 35,636

Date: September 21, 1994

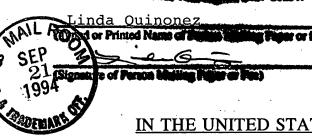
MORRISON & FOERSTER 755 Page Mill Road Palo Alto, CA 94304-1018 (415) 813-5600

Fax: (415) 494-0792

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Date of Deposit September 21, 1994

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: U.S. Patent 4,844,882

Issued: July 4, 1989

To:

Widder et al.

For:

CONCENTRATED STABILIZED

MICROBUBBLE-TYPE ULTRASONIC

IMAGING AGENT

APPLICATION FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C. SECTION 156

The Honorable Commissioner of Patents and Trademarks
Box Patent Extension
Washington, D.C. 20231

Sir:

In accordance with the provisions of 35 U.S.C. section 156, Molecular Biosystems, Inc., a corporation of the state of Delaware, having a place of business at 10030 Barnes Canyon Road, San Diego, California, 92121-2729 (hereinafter referred to as "MBI") represent that they are the assignee of the entire interest in and to Letters Patent of the United States No. 4,844,882 granted to Kenneth J. Widder and Peter J. Westkaemper for CONCENTRATED STABILIZED MICROBUBBLE-TYPE ULTRASONIC IMAGING AGENT by virtue of an assignment in favor of MBI, recorded on January 21, 1988, Reel 4834, Frames 803. See Appendix Tab A for a copy of the assignment. This application is submitted by Applicant's authorized agent as set forth in 37 C.F.R. section 1.730. See Appendix Tab B for a copy of the Power of Attorney authorizing the undersigned to act in this manner. Applicant hereby submits this application for extension of patent term under 35 U.S.C.

94 SEP 23 AM 9: 2

section 156 by providing the following information as set forth in 37 C.F.R. section 1.740.

- (1) The approved product is identified as ALBUNEX® which is used for ultrasonic imaging in medical procedures. ALBUNEX® comprises a suspension of albumin microspheres which is produced by sonication of a 5% solution of human albumin.
 - (2) The approved product was subject to regulatory review under Section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360(e)).
 - (3) The approved product received permission for commercial marketing and use under Section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360(e)) on August 5, 1994.
 - (4) This Application of extension of the patent term under 35 U.S.C. section 156 is being submitted within the statutory 60 day period, said period will expire on October 4, 1994.
 - (5) The complete identification of the patent for which extension is being sought is as follows:

Inventors: Kenneth J. Widder and Peter J. Westkaemper

Patent Number: 4,844,882

Issue Date: July 4, 1989

Expires: July 4, 2006

- (6) See Appendix Tab C for a copy of the patent identified in Paragraph (5) hereof.
- (7) A receipt of maintenance fee payment has been issued with regard to U.S. Patent No. 4,844,882. A copy of the maintenance fee receipt is attached as Appendix Tab D. No disclaimer, reexamination certificate or Certificate of Correction have been issued in connection with U.S. Patent No. 4,844,882.

STATEMENT PURSUANT TO 37 CFR 1.740(a)(9)

(8) U.S. Patent 4,844,882 claims the approved product. Claims 1-8 describe a microbubble-type imaging agent which is the approved product. The manner in which each applicable patent claim reads on the approved products is as follows:

Claim 1 of U.S. Patent No. 4,844,882 claims a concentrated, storable ultrasonic imaging agent, comprising an aqueous parenteral medium containing a dispersion of microspheres predominantly of diameters less than 10 microns, said microspheres consisting of gas microbubbles enclosed by solid walls formed from heat-insolubilized biocompatible material, said imaging agent having a homogeneously dispersed concentration of greater than 1 x 10⁸ microspheres per milliliter for over 4 weeks at a temperature of 20° to 25°C.

ALBUNEX® consists of microspheres that have diameters from 1 to 9 microns. These microspheres consist of gas microbubbles enclosed by solid walls formed from heat-insolubilized human serum albumin, a biocompatible protein. ALBUNEX® has a homogeneously dispersed concentration of 3 to 5 X 108 microspheres per milliliter. The concentration of microspheres in said medium is greater than 1 X 108 microspheres per milliliter for over 4 weeks at a temperature of 20 to 25 °C. Therefore, claim 1 embraces the product ALBUNEX®.

<u>Claim 2</u> of U.S. Patent No. 4,844,882 claims an imaging agent of claim 1 in which said biocompatible material is a heat sensitive protein.

ALBUNEX® contains human serum albumin. Human serum albumin is a heat sensitive protein. Therefore, claim 2 embraces the product ALBUNEX®.

<u>Claim 3</u> of U.S. Patent No. 4,844,882 claims an imaging agent of claims 1 and 2 in which at least 80% of said microspheres have diameters in the range from 1 to 9 microns.

Microspheres having diameters in the range from 1 to 9 microns are suitable for intravenous administration. Human serum albumin produces microspheres having a diameter in the range from 1 to 9 microns. Therefore, claim 3 embraces the product ALBUNEX®.

<u>Claim 4</u> of U.S. Patent No. 4,844,882 claims an imaging agent of claim 1 in which said biocompatible material is human serum albumin.

ALBUNEX® consists of human serum albumin. Human serum albumin is available commercially as a sterile 5% aqueous solution, which can be used directly as the starting material for preparing the microspheres. Thus, claim 4 embraces the product ALBUNEX®.

<u>Claim 5</u> of U.S. Patent No. 4,844,882 claims imaging agents of claims 1 or 4 in which said gas is air.

ALBUNEX® contains microspheres which consist of gas microbubbles encapsulated in human serum albumin. When the sonication is carried out in contact with air as the ambient atmosphere, the microspheres have air centers. Air is believed to be the most convenient ambient atmosphere.

Therefore, claim 5 embraces the product ALBUNEX®.

Claim 6 of U.S. Patent No. 4,844,882 claims a concentrated, storable ultrasonic imaging agent comprising an aqueous parenteral medium containing a dispersion of microspheres at least 80% of which have diameters in the range of 1 to 9 microns, said microspheres consisting of gas microbubbles enclosed by solid walls formed from heat-insolubilized protein, said imaging agent having a homogeneously dispersed concentration of greater than 1 x 108 microspheres per milliliter, said microspheres being stabilized in said medium as evidenced by maintaining a concentration of greater than 1 x 108 microspheres per milliliter for over 4 weeks at a temperature of 20° to 25°C.

ALBUNEX® consists of microspheres that have diameters from 1 to 9 microns. These microspheres consist of gas microbubbles enclosed by solid walls formed from human serum albumin, a heat-insolubilized protein. ALBUNEX® has a homogeneously dispersed concentration of 3 to 5 X 108 microspheres per milliliter. The concentration of microspheres in said medium is greater than 1 X 108 microspheres per milliliter for over 4 weeks at a temperature of 20 to 25°C. Therefore, claim 6 embraces the product ALBUNEX®.

<u>Claim 7</u> of U.S. Patent No. 4,844,882 claims an imaging agent of claim 6 in which said protein is human serum albumin and said gas is air.

ALBUNEX® contains microspheres that consist of gas microbubbles encapsulated by human serum albumin. When the sonication is carried out in contact with air as the ambient atmosphere, the microspheres have air centers. Air is believed to be the most convenient ambient atmosphere. Therefore, claim 7 embraces the product ALBUNEX®.

<u>Claim 8</u> of U.S. Patent No. 4,844,882 claims an imaging agent of claims 6 or 7 in which said medium is an aqueous solution of the protein of the microsphere walls. The walls of the microspheres contained in ALBUNEX® are formed from human serum albumin. Claim 8 describes an imaging agent that has a medium that is an aqueous solution of the protein of the microspheres. The human serum albumin is a solution protein of the microsphere. Therefore, claim 8 embraces the product ALBUNEX®.

STATEMENT PURSUANT TO 37 CFR 1.740(a)(10)

- (9) The relevant dates and information, pursuant to 35 USC §156(g), to enable the Secretary of Health and Human Services to determine the applicable regulatory review period are as follows:
- (i) As shown in "Appendix E," the Investigational Device Exemption for Albunex™ was filed on August 18, 1987.
 - (ii) The application for product approval was submitted September 11, 1990.
- (iii) The application was approved by the Food and Drug Administration August 5, 1994.

STATEMENT PURSUANT TO 37 CFR §1.740(a)(11)

(9) As a brief description of the activities undertaken by the marketing applicant, MBI, during the applicable regulatory review period as set forth in 37 CFR §1.704(a)(11), attached hereto as "Appendix E" is a chronology of the major communications between MBI and the FDA from about August 18, 1987 until about August 5, 1994.

STATEMENT PURSUANT TO 37 CFR §1.740(a)(12)

- (10) Applicant is of the opinion that U.S. Patent No. 4,844,882 is eligible for extension under 35 U.S.C. section 156 because it satisfies all the requirements for such extensions as follows:
 - (a) 35 U.S.C. section 156(a)
 U.S. Patent No. 4,844,882 claims a method of ultrasonic imaging using the approved product, ALBUNEX®.
 - (b) 35 U.S.C. section 156(a)(1)The term of U.S. Patent No. 4,844,882 has not expired before submission of this application.
 - (c) 35 U.S.C. section 156(a)(2)

 The term of U.S. Patent No. 4,844,882 has never been extended.
 - (d) 35 U.S.C. section 156(a)(3)

 The application for extension is submitted by MBI, an assignee of the entire interest of U.S. Patent No. 4,844,882. See Appendix Tab A.
 - (e) 35 U.S.C. section 156(a)(4)

 The product, ALBUNEX®, has been subject to a regulatory review period before its commercial marketing or use.
 - (f) 35 U.S.C. section 156(a)(5)(a)

 The commercial marketing or use of the product, ALBUNEX®, after the regulatory review period is the first permitted commercial marketing or use of the product under the provision of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. section 355) under which such regulatory period occurred.
- (11) The length of extension of the patent term of U.S. Patent No. 4,844,882, claimed by MBI is 2.09 years or 763 days. The length of the extension was determined as follows:
- (a) The regulatory review period under 35 U.S.C. section 156(g)(3)(A) as set forth in 37 CFR §1.777(c)(1), the testing period, which began August 18, 1987, with the filing of the IDE and ended with the submission of the request for product approval on September 11, 1990 which is 3.07 years or 1121 days, and in §1.777(c)(2), the approval period, which began September 11, 1990, with the submission of the request for product approval and ended August 5, 1994 with the approval of the product which is 3.90 years or 1425 days and is a total of 6.72 years or 2545 days.
- (i) The period of review under 37 CFR §1.777(c)(1), the testing period, was from August 18, 1987 to September 11, 1990, which is 3.07 years or 1121 days.

- (ii) The period of review under 37 CFR §1.777(c)(2), the approval phase, was from September 11, 1990 to August 5, 1994, which is 3.90 years or 1425 days.
- (b) The regulatory review period upon which the period of extension is calculated is the entire regulatory review period as determined in sub-paragraph 11(a) above (2545 days) less the sum of:
- (i) The number of days in the regulatory period as set forth in $\S1.777(c)(1)$ and (2) which were on and before the date on which the patent issued (2545 686 = 1858 days);
- (ii) The number of days in the regulatory period as set forth in $\S1.777(c)(1)$ and (2) during which MBI did not act with due diligence, which is zero (0) days (1858 0 = 1858); and
- (iii) One-half the number of days remaining in the testing period as set forth in $\S1.777(c)(1)$ after the patent issued (July 4, 1989) (1121 687 = 434 ÷ 2 = 217 days) (1858 217 = 1641);

which is a total of 4.49 years or 1641 days.

- (c) The number of days as determined in 11(b) above, i.e., 1641 days, when added to the original term of the patent which is July 4, 2006 would result in the date December 31, 2010.
- (d) The addition of fourteen (14) years to the date of approval of the application under §515 of the Federal Food, Drug and Cosmetic Act would result in the date August 5, 2008.
 - (e) When comparing 11(c) and (d) above, the earlier date is August 5, 2008.
- (f) Since the original patent issued after September 24, 1984, and since no request for exemption under subsection (5)(f) of §515 of the Federal Food, Drug and Cosmetic Act was submitted before September 24, 1984, five (5) years when added to the original expiration date of the patent (July 4, 2006) would result in the date July 4, 2011.
- (g) The earlier date when comparing 11(c) and (f) above is August 5, 2008. Therefore, the length of extension of patent term claimed by MBI is 763 days or 2.09 years.

STATEMENT PURSUANT TO 37 CFR §1.740(a)(13)

- (12) Applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services any information which is material to any determinations to be made relative to the application for extension.
- (13) The prescribed fee for receiving and acting upon this application is enclosed. If any additional fees are due, authorization is given to charge our deposit account number 03-1952.
 - (14) Direct all inquiries and correspondence relating to this application to

Freddie K. Park Morrison & Foerster 755 Page Mill Road Palo Alto, CA 94304 Phone: (415) 813-5705

Fax:

(415) 494-0792

- (15) A certified duplicate of this application is being submitted herewith.
- (16) The requisite declaration pursuant to 37 CFR §1.740(b) is attached hereto as Appendix F.

Respectfully submitted,

Freddie K. Park

Registration No. 35 636

Date September 21, 1994

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Fax: (415) 494-0792

TILTON, FALLON, LUNGMUS & CHESTNUT 100 SO. WACKER DR. CHICAGO, IL 60606-4002



"TILTON, FALLON, LUNGMUS, CHESTNUT

UNITED STATES PATENT AND TRADEMARK OFFICE NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

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HE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF HE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS VAILABLE AT THE U.S. PATENT AND TRADEMARK OFFICE ON THE REEL AND FRAME UMBER REFERENCED BELOW. A DIGEST OF THE DOCUMENT HAS ALSO BEEN MADE NO APPEARS IN THE OFFICE'S RECORDS AS SHOWN:

ISSIGNOR: OOT WIDDER, KENNETH J.

SSIGNOR: 002 WESTKAEMPER, PETER J.

DOC DATE: 12/29/87 DOC DATE: 12/29/87

ECORDATION DATE: 01/21/88 NUMBER OF PAGES OOL REEL/FRAME 4834/0803

IGEST: ASSIGNMENT OF ASSIGNORS INTEREST

SSIGNEE: 501 MOLECULAR BIOSYSTEMS, INC., SAN DIEGO, CA. A CORP. OF CA.

ERIAL NUMBER ATENT NUMBER

7-139576

FILING DATE 12/29/87

ISSUE DATE 00/00/00

FITLE OF INVENTION: CONCENTRATED STABILIZED MICROBUBBLE-TYPE ULTRASONI

IMAGING AGENT

INVENTOR: OOI WIDDER, KENNETH J. NVENTOR: 002 WESTKAEMPER, PETER J.

SERIAL NUMBER 7-139576 PATENT NUMBER

FILING DATE 12/29/87 ISSUE DATE 00/00/00

BITLE OF INVENTION: CONCENTRATED STABILIZED MICROBUBBLE-TYPE ULTRASONI ■ IMAGING AGENT

MNVENTOR: OOI WIDDER, KENNETH J. INVENTOR: 002 WESTKAEMPER, PETER J.

EXHIBIT A

accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

10 Other

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EXAMINER'S ACTION

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EXAMINER'S ACTION

Exhibits

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Patent of: Widder et al

Patent Number: 4,844,882

Issued: July 4, 1989

For: CONCENTRATED STABILIZED MICROBUBBLE-TYPE ULTRASONIC IMAGING AGENT

POWER OF ATTORNEY

The Honorable Commissioner of Patents and Trademarks BOX PATENT EXTENSION Washington, DC 20231

Dear Sir:

In the matter of the above-entitled application, I hereby revoke all power of Attorney heretofore given by me and appoint as my attorney Freddie K. Park, Reg. No. 35,636; Reid G. Adler, Reg. No. 30,988; Felissa H. Cagan, Reg. No. 35,089; Thomas E. Ciotti, Reg. No. 21,013; Patricia M. Drost, Reg. No. 29,790; Edward G. Durney, Reg. No. 37,611; Tyler Dylan, Reg. No. 37,612; Nancy Joyce Gracey, Reg. No. 28,216; Bill Kennedy, Reg. No. 33,407; Paul C. Kimball, Reg. No. 34,641; Susan K. Lehnhardt, Reg. No. 33,943; Shmuel Livnat, Reg. No. 33,949; Gladys H. Monroy, Req. No. 32,430; Kate H. Murashige, Req. No. 29,959; Jackie N. Nakamura, Reg. No. 35,966; Paul F. Schenck, Reg. No. 27,253; Lynn E. Schwenning, 37,233; James R. Shay, 32,062; Debra A. Shetka, Reg. No. 33,309; Cecily Anne Snyder, Reg. No. 37,448; E. Thomas Wheelock, Reg. No. 28,825; and Anna Lewak Wight, Reg. No. 33,006, all of Morrison & Foerster, 755 Page Mill Road, Palo Alto, California 94304, with full power of substitution, association and revocation, to prosecute said application and to transact all business in the Patent Office connected therewith.

EXHIBIT B

Please direct all telephone calls to Freddie K. Park at telephone number (415) 813-5600.

MOLECULAR BIOSYSTEMS, INC. Assignee of Record

Dated: September 19, 1994

Ву

Name: Steven Lawson

Title: Vice President, Legal Affairs

CERTIFICATE OF MAILING BY "EXPRESS MAIL"

"Express Mail" mailing label number TB 028723310 US

Date of Deposit September 21, 1994

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner of patents and Trademarks, Washington, D.C. 20231

(Typed or printed name of person mailing paper or fee)

(Signature of person mailing paper or fee)

CERTIFICATE UNDER 37 CFR 3.73(b)

Applicant:	Widder et al
Patent No.:	4,844,882 Issued: <u>July 4, 1989</u>
For: <u>CONCEN</u> AGENT	NTRATED STABILIZED MICROBUBBLE-TYPE ULTRASONIC IMAGING
MOLECULAR E	CORPORATION (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)
certifies that it is the	assignee of the entire right, title and interest in the patent application identified above by virtue of
	nt from the inventor(s) of the patent application identified above. The assignment was recorded in the ademark Office at Reel 4834, Frame 0803, or for which a copy thereof is attached.
OR	
B.[] A chain of title below:	le from the inventor(s), of the patent application identified above, to the current assignee as shown
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	o: nent was recorded in the Patent and Trademark Office at Reel, Frame, or for which a copy thereof is
[] Additional	documents in the chain of title are listed on a supplemental sheet.
[X] Copies of assign	ments or other documents in the chain of title are attached.
	reviewed all the documents in the chain of title of the patent application identified above and, to the sknowledge and belief, title is in the assignee identified above.
The undersigned (wh	nose title is supplied below) is empowered to act on behalf of the assignee.
and belief are believe statements, and the li	all statements made herein of my own knowledge are true, and that all statements made on information ed to be true; and further, that these statements are made with the knowledge that willful false ike so made, are punishable by fine or imprisonment, or both, under Section 1001, Title 18 of the and that such willful false statements may jeopardize the validity of the application or any patent issuing
Date: _	September 19, 1994
Name: _	Steven Lawson
Title: _	Vice President, Legal Affairs
Signature:	Stewn as 20

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EXAMINER'S ACTION

Patent Number: [11]

4,844,882

Date of Patent: [45]

Jul. 4, 1989

[54]	CONCENTRATED STABILIZED
	MICROBUBBLE-TYPE ULTRASONIC
	IMAGING AGENT

[75]	Inventors:	Kenneth J. Widder, Del Mar; Peter J. Westkaemper, San Diego, both of Calif.
		Calif.

		Calif.
[73]	Assignee:	Molecular Biosystems, Inc., San Diego, Calif.
[21]	Appl. No.:	139,576

[22]	Filed:	Dec. 29, 1987
[51]	Int. Cl.4	A61K 49
[52]	U.S. Cl	424/9; 514/
_	Field of S	128/66

[52]	U.S. Cl.	. 424/9; 514/945;
	Field of Search	128/660.01
		128/660_663

[56]	References Cited	
	U.S. PATENT DOCUMENTS	

4.276,885	7/1981	Tickner et al.	129/660
4,400,442	8/1984	Hilmann et al	170/663
4,3/4,203	4/1986	Feinstein	170/661
4,/18,433	1/1988	Feinstein	120/660
4,774,958	10/1988	Feinstein	/660.01

OTHER PUBLICATIONS

Tickner et al., National Technical Information Service Report HR 62917-1A, Apr. 1977, pp. 34-40. Feinstein et al., (1984), J. Am. Coll. Cardio., 3:14-20. Keller et al., (1987), Amer. Heart J., 114:570-575.

Primary Examiner-Douglas W. Robinson Assistant Examiner—Raymond J. Henley, III Attorney, Agent, or Firm-Tilton, Fallon, Lungmus & Chestnut

[57] **ABSTRACT**

A microbubble-type ultrasonic imaging agent is provided comprising a parenterally-administerable aqueous medium containing a dispersion of microspheres predominantly of diameters less than 10 microns, wherein the microspheres consist of gas microbubbles encapsulated with water-insolubilized biocompatible material. The imaging agent is characterized by having a concentration of greater than 100×106 microspheres per milliliter, and a stability such that this concentration is maintained for over 4 weeks at a temperature of 20° to 25° C.

8 Claims, 4 Drawing Sheets

PAYOR NUMBER 000131

TILTON, FALLON, LUNGMUS & CHESTNUT 100 SOUTH WACKER DRIVE. SUITE 960 HARTFORD PLAZA CHICAGO, IL 60606-4002

DATE MAILED 10/29/92

275608

MAINTENANCE FEE STATEMENT

The data shown below is from the records of the Patent and Trademark Office. If the maintenance fees and any necessary surcharges have been timely paid for the patents listed below, the notation "PAID" will appear in column 10, "status" below.

If a maintenance fee payment is defective, the reason is indicated by code in column 10, "status" below. An explanation of the codes appears on the reverse of the Maintenance Fee Statement. TIMELY CORRECTION IS REQUIRED IN ORDER TO AVOID EXPIRATION OF THE PATENT. NOTE 37 CFR 1.377. THE PAYMENT(S) WILL BE ENTERED UPON RECEIPT OF ACCEPTABLE CORRECTION. IF PAYMENT OR CORRECTION IS SUBMITTED DURING THE GRACE PERIOD, A SURCHARGE IS ALSO REQUIRED. NOTE 37 CFR 1.20(k) and (i).

If the statement of small entity status is defective the reason is indicated below in column 10 for the related patent number. THE STATEMENT OF SMALL ENTITY STATUS WILL BE ENTERED UPON RECEIPT OF ACCEPTABLE CORRECTION.

				 SERIAL NUMBER					
1	4,844,882	283	450	 07/139,576	07/04/89	12/29/87	04	YES	PAID

If the "status" column for a patent number listed above does not indicate "PAID" a code or an asterisk (*) will appear in the "status" column. Where an asterisk (*) appears, the codes are set out below by the related item number. An explanation of the codes indicated in the "status" column and as set out below by the related item number appears on the reverse of the maintenance fee statement.

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EXHIBIT D

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Exhibit E

DATE	SUBJECT MATTER	ACTIVITY	COMMENTS
	IDE G870144		
8/18/87	ORIGINAL	Submission to FDA	Submission of Original IDE containing Protocol 1200
8/24/87	IDE G870144	Latter from EDA	EDA account of IDE and the state of IDE
0/24/0/	IDE G870144	Letter from FDA	FDA receipt of IDE and assignment of IDE number
9/1/87	Amendment 1	Submission to FDA	Doguest for literature reference
3/1/0/	Amendment	Submission to FDA	Request for literature references
9/18/87	IDE G870144	Letter from FDA	Request for additional information regarding Protocol 12001
0,10,0,	102 0070144	Letter Hom I DA	Letter stating that product would be reviewed as a
10/13/87	IDE G870144	Letter from FDA	device
	IDE G870144		
10/20/87	Amendment 2	Submission to FDA	Response to 9/18/87 letter from FDA
,,_	IDE G870144		Request for additional information regarding Protocol
11/20/87	Amendment 2	Letter from FDA	12001
	IDE G870144		12001
12/9/87	Amendment 3	Submission to FDA	Response to 11/20/87 letter from FDA
	IDEG870144		Request for additional information regarding Protocol
1/14/88	Amendment 3	Letter from FDA	12001
	IDE G870144		
1/22/88	Supplement 1	Submission to FDA	Response to 1/14/88 letter from FDA
2/3/88	IDE G870144	Telephone Call with FDA	Discussion regarding 9/18/87 letter from FDA
	IDE G870144		
2/8/88	Supplement 2	Submission to FDA	Follow-up to 2/3/88 telephone call with FDA
	IDEG870144		Conditional approval of Protocol 12001 and request
2/23/88	Amendment 3	Letter from FDA	for additional information
,	IDE G870144		,
4/13/88	Supplement 3	Submission to FDA	Addition of new investigator to Protocol 12001
	IDE G870144		
4/22/88	Supplement 4	Submission to FDA	Addition of Protocol 12002
	IDE G870144		
5/12/88	Supplement 5	Submission to FDA	Addition of Protocol 12003
	IDEG870144		Request for additional information regarding Protocol
5/13/88	Supplement 4	Letter from FDA	12002
	IDE G870144		
5/27/88	Supplement 6	Submission to FDA	Response to 5/13/88 letter from FDA
	IDE G870144		Request for additional information regarding Protocol
6/9/88	Supplement 5	Letter from FDA	12003
	IDE G870144		Progress Report and request for approval of Protocol
6/15/88	Supplement 7	Submission to FDA	12002, and addition of Protocol 12005
			Request for additional information regarding Protocol
6/15/88	IDE G870144	Letter from FDA	12002
6/23/88	Supplement 4	Letter from FDA	Conditional approval of Protocols 12001and 12002
	IDE G870144		Notification of internal review board approval for
7/11/88	Supplement 8	Submission to FDA	Protocol 12001 and request to add second site
	IDE G870144		Request for additional information regarding Protocol
	1:	•	- Interpretation accommendation regarding interpretation

APPENDIX E

7/24/88	IDE G870144	Letter to FDA	Request for permit to export to the Netherlands
	IDE G870144		
8/4/88	Supplement 8	Letter from FDA	Approval to add second site to Protocol 12001
			Notification that clinical trials in the Netherlands could
9/8/88	IDE G870144	Letter from FDA	be acceptable
	IDE G870144		Progress Report and response to 7/15/88 letter from
9/21/88	Supplement 9	Submission to FDA	FDA
		İ	Conditional approval of Protocol 12005 and request
10/21/88	IDE G870144	Letter from FDA	for additional information
4 4 4 0 40 0	IDE G870144		
11/16/88	Supplement 10	Submission to FDA	Response to 10/21/88 letter from FDA
12/16/88	IDE G870144	Letter from FDA	Approval of Protocol 12005
40/40/00	IDE 0070444	T. I. O. II. 11 EDA	Request for a meeting to review facility plans with
12/16/88	IDE G870144	Telephone Call with FDA	FDA
1 /1 0 /00	IDE G870144	Cubaciacian de EDA	Addition of the state of the st
1/10/89	Supplement 11 IDE G870144	Submission to FDA	Addition of investigators and sites to Protocol 12005
1/11/89	IDE G870144	Meeting with FDA	Meeting with FDA regarding facility plans
1/11/89	Supplement 12	Submission to EDA	Correction to 1/10/89 submission to FDA
1/11/8 3 1/24/89	IDE G870144	Submission to FDA Meeting with FDA	
1/24/03	IDE G870144	Meeting With FDA	Discussion regarding manufacturing process
2/9/89	Supplement 11	Telephone Call with FDA	Request for status of 1/10/89 submission to FDA
2/3/03	Supplement 11	Telephone Call With FDA	Conditional approval of Protocol 12005 as
	IDE G870144		supplemented on 1/10/89 and request for additional
2/9/89	Supplement 11 & 12	Letter from FDA	information
213103	Supplement 11 d 12	Letter Hom FDA	intomation
2/9/89	IDE G870144	Telephone Call with FDA	Inquiry into which OB/Gyn division would review IDE
<u>,</u>	IDE G870144	Tolophono Gail Wall 1874	inquiry into winch objeyir division would review ibb
2/23/89	Supplement 13	Submission to FDA	Response to 2/9/89 letter from FDA
2/23/89	IDE G870144	Telephone Call with FDA	Discussion regarding clinical investigations
2/28/89	IDE G870144	Telephone Call from FDA	Follow-up to 2/23/89 telephone call with FDA
	IDE G870144		Discussion regarding 1/10/89 and 2/23/89
3/18/89	Supplement 11 & 13	Telephone Call with FDA	submissions to FDA
	IDE G870144		Conditional approval of Protocol 12005 and request
3/20/89	Supplement 13	Letter from FDA	for additional information
	IDEG870144		
3/20/89	Supplement 13	Telephone Call with FDA	Discussion regarding 3/20/89 letter from FDA
4/4/89	IDE G870144	Letter to FDA	Request for permit to export to Japan
4/4/89	IDE G870144	Letter to FDA	Request for permit to export to the Netherlands
	IDE G870144		
4/7/89	Supplement 14	Submission to FDA	Notification of current list of investigators
4/11/89	IDE G870144	Letter to FDA	Request for permit to export to Norway
			Acknowledgement of receipt of 4/4/89 and 4/5/89
			letters regarding requests for permit to export to
4/14/89	IDE G870144	Letter from FDA	Japan and the Netherlands
•			
4/14/89	IDE G870144	Telephone Call with FDA	Request for meeting with FDA regarding status of IDE
	IDE G870144		Request to extend deadline to respond to 3/20/89
4/20/89	Supplement 15	Submission to FDA	letter from FDA

	IDE G870144		
5/2/89	Supplement 13	Meeting at FDA	Discussion regarding 3/20/89 letter from FDA
			Notification that processing of requests takes 4-6
5/5/89	IDE G870144	Letter from FDA	weeks after receipt by FDA
	IDE G870144		
5/16/89	Supplement 13	Telephone Call with FDA	Request for minutes of 5/2/89 meeting with FDA
	IDE G870144		
5/16/89	Supplement 13	Letter to FDA	Minutes of 5/2/89 meeting with FDA
	IDE G870144		Approval of request to extend deadline for response
5/16/89	Supplement 15	Letter from FDA	to 3/20/89 letter from FDA
· .			
5/18/89	IDE G870144	Letter to FDA	Request for status of export permit to the Netherlands
			Approval of request for permit to export to Japan and
5/24/89	IDE G870144	Letter from FDA	Norway
5/28/89	IDE G870144	Letter from FDA	Export permits for Japan and Norway
	IDE G870144		
6/5/89	Supplement 16	Submission to FDA	Response to 3/20/89 letter from FDA
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6/6/89	Supplement 17	Submission to FDA	Progress Report
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6/22/89	Supplement 18	Submission to FDA	Progress Report
0,,	IDE G870144	Commoditi to 1 D/1	1 Togress Report
6/23/89	Supplement 16 & 17	Telephone Call with FDA	Discussion regarding clinical protocols
0,20,00	IDE G870144	Telephone can with 1 bA	Discussion regarding clinical protocols
6/29/89	Supplement 19	Submission to FDA	Addition of Protocol 12007
0/20/00	IDE G870144	Oddinission to 1 DA	Addition of Protocol 12007
7/11/89	Supplement 20	Submission to FDA	Addition of Protocol 12006
7/11/89	IDE G870144	Letter from FDA	Notification of FDA relocation
7/14/03	IDE G870144	Letter from FDA	ivotification of PDA relocation
7/14/00	1	Latter from EDA	Assessed of December 19905
7/14/89	Supplement 16	Letter from FDA	Approval of Protocol 12005
	IDE 0070444	•	
0/44/00	IDE G870144		Acknowledgement of receipt of 6/22/89 submission
8/11/89	Supplement 18	Letter from FDA	to FDA and request for additional information
0 /4 0 /00	IDE G870144		Conditional approval of Protocols 12006 and 12007
8/16/89	Supplement 19 & 20	Letter from FDA	and request for additional information
			Discussion regarding PMA, termination of Protocol
9/14/89	IDE G870144	Meeting at FDA	12003 and changes to Protocols 12006 and 12007
	IDE G870144	·	Response to 8/11/89 letter from FDA regarding
9/21/89	Supplement 21	Submission to FDA	6/22/89 submission to FDA
	IDE G870144		Response to 8/16/89 Letter from FDA regarding
9/28/89	Supplement 22	Submission to FDA	Protocols 12006 and 12007
			Discussion regarding software analysis of ultrasound
10/17/89	IDE G870144	Meeting at FDA	images
			Conditional approval of Protocol 12006 and request
10/20/89	IDE G870144	Letter from FDA	for additional information
1			Arrange for meeting at FDA regarding software
10/20/89	IDE G870144	Telephone Call with FDA	analysis of ultrasound images

	IDE G870144		: -
11/2/89	Supplement 23	Submission to FDA	Request for change to manufacturing process
	IDE G870144		Request for status of 11/2/89 submission to FDA and
11/17/89	Supplement 23	Telephone Call with FDA	request for meeting at FDA to discuss
	IDE G870144		
11/20/89	Supplement 22	Letter from FDA	Approval of Protocol 12007
11/28/89	IDE G870144	Meeting at FDA	Discussion regarding 11/2/89 submission to FDA
	IDE G870144		
12/4/89	Supplement 24	Submission to FDA	Addition of Protocol 12004
	IDE G870144	•	Request to expand Protocol 12007 to additional
12/6/89	Supplement 25	Submission to FDA	patients
			Request for additional information regarding export
12/10/89	IDE G870144	Letter from FDA	permit to the Netherlands
	IDE G870144		Approval of change to manufacturing process as
12/29/89	Supplement 23	Letter from FDA	requested in 11/2/89 submission to FDA
•	IDE G870144		Approval of Protocol 12004 as amended in 12/4/89
12/29/89	Supplement 24	Letter from FDA	submission to FDA
·	IDE G870144		
1/4/90	Supplement 26	Submission to FDA	Addition of Protocol 13289
	-		Approval of request to expand Protocol 12007 to
	IDE G870144		additional patients as requested in 12/6/89
2/5/90	Supplement 25	Letter from FDA	submission to FDA
	IDE G870144		
2/7/90	Supplement 27	Submission to FDA	Summary of clinical investigators and sites
	IDE G870144		·
2/9/90	Supplement 28	Submission to FDA	Information regarding animal studies
·	IDE G870144		Conditional approval of Protocol 13289 and request
2/12/90	Supplement 26	Letter from FDA	for additional information
2/22/90	IDE G870144	Telephone Call from FDA	Request for minutes of 11/17/89 meeting at FDA
2/22/90	IDE G870144	Letter to FDA	Request for permit to export to Japan
			Request for permit to export to Japan
3/14/90	IDE G870144	Letter to FDA	,
	IDE G870144		
3/16/90	Supplement 29	Submission to FDA	Response to 2/12/90 letter from FDA
3/21/90	IDE G870144	Telephone Call with FDA	Discussion regarding 2/9/90 submission to FDA
3/21/90	IDE G870144	Letter to FDA	Request for permit to export to the Netherlands
4/3/90	IDE G870144	Letter to FDA	Request for permit to export to Norway
	IDE G870144		Conditional approval of Protocol 13289 and request
4/18/90	Supplement 29	Letter from FDA	for additional information
,			Discussion regarding status of IDE and upcoming
4/18/90	IDE G870144	Telephone Call with FDA	meeting with FDA
4/18/90	IDE G870144	Letter from FDA	Approval of request for permit to export to Japan
	IDE G870144		Response to 4/18/90 Letter from FDA regarding
5/11/90	Supplement 30	Submission to FDA	Protocol 13289
	IDE G870144		
5/18/90	Supplement 31	Submission to FDA	Correction to 5/11/90 submission to FDA

	IDE G870144		
6/1/90	Supplement 32	Submission to FDA	Progress Report
	IDE G870144		
6/5/90	Supplement 33	Submission to FDA	Correction to 6/1/90 submission to FDA
6/12/90	PMA P900059	Letter to FDA	Agenda for upcoming meeting withFDA
	IDE G870144		Conditional approval of Protocol 13289 and request
6/14/90	Supplement 30 & 31	Letter from FDA	for additional information
6/20/90	PMA	Telephone Call with FDA	Discussion upcoming meeting with FDA
6/27/90	PMA	Meeting with FDA	Discussion regarding filing of PMA
•	IDE G870144		Approval of Protocol 13289 and request for additional
7/3/90	Supplement 30 & 31	Letter from FDA	information
	IDE G870144		
7/5/90	Supplement 33	Letter from FDA	Comments on 6/1/90 and 6/5/90 submissions to FDA
7/9/90	IDE G870144	Telephone Call with FDA	Discussion regarding clinical information
7/17/90	PMA	Telephone Call with FDA	Follow-up to 6/27/90 meeting with FDA
7/24/90	IDE G870144	Telephone Call with FDA	Discussion regarding export request for Norway
7/24/90	IDE G870144	Letter to FDA	Request for permit to export to the Netherlands
8/2/90	IDE G870144	Letter to FDA	Request for permit to export to Norway
8/2/90	IDE G870144	Letter from FDA	Request for manufacturing and clinical information
•	PMA P900059		
9/11/90	ORIGINAL	Submission to FDA	Submission of Original PMA
	IDE G870144		
9/13/90	Supplement 34	Submission to FDA	Response to 7/3/90 letter from FDA
	IDE G870144		See IDE G870144/Supplement 34: Logged in by FDA
9/13/90	Supplement 35	Submission to FDA	as Supplement 35
			Request for additional information regarding 6/1/90
9/17/90	IDE G870144	Letter from FDA	Progress Report
9/26/90	PMA P900059	Telephone Call with FDA	Discussion regarding PMA
9/27/90	PMA P900059	Telephone Call with FDA	Request for status of 9/13/90 submission to FDA
9/28/90	PMA P900059	Telephone Call with FDA	Request for status of PMA
	PMA P900059		
9/28/90	Amendment 1	Submission to FDA	Follow-up to 9/26/90 telephone call with FDA
	PMA P900059		Additional follow-up to 9/26/90 telephone call with
10/2/90	Amendment 2	Submission to FDA	FDA
10/11/90	PMA P900059	Telephone Call with FDA	Discussion regarding status of PMA
10/12/90	PMA P900059	Telephone Call with FDA	Discussion regarding status of PMA
10/16/90	PMA P900059	Telephone Call with FDA	Discussion regarding use of statistical data in PMA
· · · · · · · · · · · · · · · · · · ·			Additional discussion regarding use of statistical data
10/19/90	PMA P900059	Telephone Call with FDA	in PMA
			Request for status of internal FDA meeting regarding
10/22/90	PMA P900059	Telephone Call with FDA	PMA
			Discussion regarding manufacturing process and
10/23/90	PMA P900059	Telephone Call with FDA	status of "fileability" of PMA
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10/24/90	PMA P900059	Telephone Call with FDA	Additional discussion regarding manufacturing process
. 512 1100		1. C. Opinono Can With 1 DA	resistant diseason regularing manarastaning process
10/26/90	PMA P900059	Telephone Call with FDA	Additional discussion regarding manufacturing process
13/23/33	1	1 Copholic Can With 1 DA	industrial discussion regarding manufacturing process

10/30/90	PMA P900059	Telephone Call with FDA	Request for status of "fileability" of PMA
			Notification of "fileable" status of PMA and request
11/19/90	PMA P900059	Letter from FDA	for additional information
·			Proposed outline for amendment to statistical data
11/27/90	PMA P900059	FAX to FDA	used in PMA
			Discussion regarding response to 11/20/90 letter from
11/28/90	PMA P900059	Telephone Call with FDA	FDA
			Discussion regarding status of IDE and response to
12/10/90	PMA P900059	Telephone Call with FDA	11/20/90 letter from FDA
12/17/90	IDE G870144	Letter from FDA	Denial of request for permit to export to Norway
			Notification that request for permit to export to
1/15/91	IDE G870144	Telephone Call with FDA	Norway was denied
2/1/91	PMA P900059	Telephone Call with FDA	Notification of change of PMA reviewer at FDA
	PMA P900059		
2/1/91	Amendment 3	Submission to FDA	Response to 11/19/90 letter from FDA
2/13/91	PMA P900059	FAX to FDA	Request for status of PMA scientific review
			Notification of change of FDA reviewing division from
2/22/91	PMA P900059	FAX from FDA	cardiovascular to OB/Gyn
2/25/91	PMA P900059	Telephone Call with FDA	Discussion regarding review of PMA by OB/Gyn
2/26/91	PMA P900059	Letter to FDA	Agenda for 2/28/91 meeting at FDA
2/28/91	PMA P900059	Meeting at FDA	Discussion regarding status of PMA
3/4/91	PMA P900059	Telephone Call with FDA	Review of 2/28/91 meeting at FDA
3/25/91	PMA P900059	Telephone Call with FDA	Request for status of PMA
	PMA P900059		Additional information regarding 2/1/91 submission to
3/25/91	Amendment 4	Submission to FDA	FDA
			Approval of request for permit to export to the
3/27/91	IDE G870144	Letter from FDA	Netherlands
	`		
4/15/91	IDE G870144	Letter from FDA	Approval of request for permit to export to Norway
	IDE G870144		
4/22/91	Supplement 36	Submission to FDA	Addition of Protocol 13191
			Notification that review of PMA would take place in
5/1/91	PMA P900059	Telephone Call with FDA	90 days
5/3/91	PMA P900059	Telephone Call with FDA	Discussion regarding status of PMA
5/3/91	PMA P900059	Letter to FDA	Comments regarding review of PMA
5/6/91	PMA P900059	Telephone Call with FDA	Request for status of PMA
		<u> </u>	Request for status of PMA and inquiry regarding panel
5/23/91	PMA P900059	Telephone Call with FDA	meeting
5/23/91	PMA P900059	Telephone Call with FDA	Request for status of PMA
	IDE G870144		Conditional approval of Protocol 13191 and request
5/23/91	Supplement 36	Letter from FDA	for additional information
			Notification of intent to send PMA "filed" letter and
5/24/91	PMA P900059	Telephone Call with FDA	report on status of review of Protocol 13191
	PMA P900059		
5/31/91	Amendment 5	Submission to FDA	Notification regarding product licensee
	IDE G870144		The state of the s
6/7/91	Supplement 37	Submission to FDA	Addition of Protocol 13291
<u> </u>	100ppionione 07	13dominosion to 15A	7.55.531 017 10,000 10201

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6/7/91	Supplement 38	Submission to FDA	Response to 5/23/91 letter from FDA
6/10/91	PMA P900059	Letter from FDA	Receipt of PMA "Filed" letter
	IDE G870144		
6/11/91	Supplement 39	Submission to FDA	Progress Report
	PMA P900059		
6/11/91	Amendment 6	Submission to FDA	Notification of official PMA correspondents at MBI
	PMA P900059		The state of the s
6/14/91	Amendment 7	Letter to FDA	Progress Report
6/14/91	PMA P900059	Telephone Call with FDA	Request for status of PMA
6/18/91	PMA P900059	Telephone Call with FDA	Request for status of PMA
6/20/91	PMA P900059	Letter from FDA	Request for additional information
			Request for discussion with FDA regarding 6/20/91
6/20/91	PMA P900059	Telephone Call with FDA	letter from FDA
6/20/91	PMA P900059	Telephone Call with FDA	Discussion regarding 6/20/91 letter from FDA
	IDE G870144		Conditional approval of Protocol 13291 and request
7/11/91	Supplement 37	Letter from FDA	for additional information
7/11/91	PMA P900059	Letter from FDA	Request for additional information
	IDE G870144		
7/23/91	Supplement 36	Letter from FDA	Approval of Protocol 13191
			Discussion regarding 7/11/91 letter from FDA and
8/7/91	PMA P900059	Telephone Call with FDA	request for status of PMA
			Arrange for telephone call with FDA regarding
8/7/91	PMA P900059	Telephone Call with FDA	6/20/91 letter from FDA
			Discussion regarding 6/20/91 and 7/11/91 letters
8/8/91	PMA P900059	Telephone Call with FDA	from FDA
	PMA P900059		
8/8/91	Amendment 8	Submission to FDA	Minutes from 8/8/91 telephone call with FDA
	IDE G870144		
8/9/91	Supplement 40	Submission to FDA	Response to 7/11/91 letter from FDA
. •			
9/11/91	PMA P900059	Telephone Call with FDA	Request for information regarding PMA panel meeting
	IDE G870144		
9/11/91	Supplement 40	Letter from FDA	Approval of Protocol 13291
	PMA P900059		
9/30/91	Amendment 9	Submission to FDA	Additional response to 6/20/91 letter from FDA
10/17/91	PMA P900059	Telephone Call with FDA	Request for information regarding PMA panel meeting
	PMA P900059		
10/25/91	Amendment 10	Submission to FDA	Correction to 9/30/91 submission to FDA
	IDE G870144		
11/19/91	Supplement 41	Submission to FDA	Request for change to packaging specifications
-	IDE G870144		
12/2/91	Supplement 42	Submission to FDA	Addition of Protocol 13391
			Request for status of PMA and information regarding
		I	, ·
12/2/91	PMA P900059	Telephone Call with FDA	panel meeting
12/2/91	PMA P900059	Telephone Call with FDA	Discussion regarding status of PMA and panel

	IDE G870144		
12/13/91	Supplement 43	Submission to FDA	Additional information regarding clinical studies
	IDE G870144		Request for additional information regarding 11/19/91
12/20/91	Supplement 41	Telephone Call with FDA	submission to FDA
	IDE G920008		
12/20/91	Original	Submission to FDA	Addition of Protocol 13491
	IDE G870144		Conditional approval of 11/19/91 submission to FDA
12/20/91	Supplement 41	Letter from FDA	and request for additional information
	IDE G870144		Conditional approval of Protocol 13391 and request
12/27/91	Supplement 42	Letter from FDA	for additional information
	IDE G870144		
1/13/92	Supplement 43	Letter from FDA	Comments regarding 12/13/91 submission to FDA
1/15/92	IDE G920008	Letter from FDA	Assignment of IDE number to Protocol 13491
	IDE G870144		
1/21/92	Supplement 44	Submission to FDA	Response to 12/27/91 letter from FDA
	IDE G870144		
	Supplement 41		
	IDE G920008		Discussion regarding 12/20/91 letter from FDA,
1/22/92	PMA P900059	Telephone Call with FDA	Protocol 13491 and request for status of PMA
1/24/92	PMA P900059	Telephone Call with FDA	Discussion regarding status of PMA
	IDE G870144		
1/24/92	Supplement 45	Submission to FDA	Response to 12/20/91 letter from FDA
			Request for additional information regarding Protocol
1/29/92	IDE G920008	Letter from FDA	13491
	IDE G870144		
2/4/92	Supplement 46	Submission to FDA	Progress Report
	IDE G870144		Request for additional information regarding Protocol
2/12/92	Supplement 44	Letter from FDA	13391
2/24/92	PMA P900059	Telephone Call with FDA	Request for status of PMA
	IDE G870144		.
2/25/92	Supplement 45	Letter from FDA	Approval of 11/19/91 submission to FDA
			Agenda for 3/16/92 meeting at FDA regarding PMA
2/25/92	PMA P900059	Letter to FDA	review and panel meeting
2/28/92	PMA P900059	Telephone Call with FDA	Arrangemts for meeting at FDA
	IDE G920008		
2/28/92	Amendment 1	Submission to FDA	Response to 1/29/92 letter from FDA
:: <u>-</u>	IDE G870144		Acknowledgement of receipt of Progress Report dated
3/6/92	Supplement 46	Letter from FDA	2/4/92
3/13/92	PMA P900059	Telephone Call with FDA	Discussion regarding upcoming meeting at FDA
	IDE G870144	· · · · · · · · · · · · · · · · · · ·	
3/13/92	Supplement 47	Submission to FDA	Response to 2/12/92 letter from FDA
J, 19/02	- Sphiomont 47		Discussion regarding status of PMA and upcoming
3/16/92	PMA P900059	Meeting with FDA	panel meeting
3/21/92	PMA P900059	Letter to FDA	Minutes from 3/16/92 meeting at FDA
3/31/92	PMA P900059	Telephone Call with FDA	Discussion regarding facility inspections
3/3 1/32	IDE G920008	- Tolephone Call With 1 DA	Request for additional information regarding Protocol
3/31/92	Amendment 1	Letter from FDA	13491
3/31/32	Tumenament I	Letter Holli FDA	וטדטו

PMA P900059 PMA P900059 IDE G870144 PMA P900059	Telephone Call with FDA Letter from FDA Letter from FDA	panel meeting Updated status of PMA Notification regarding PMA status and upcoming panel
PMA P900059 IDE G870144 PMA P900059		
IDE G870144 PMA P900059	Letter from FDA	- INVUINCATION TOUGHTUNE FIVE STATES AND UNCOMING NAME
IDE G870144 PMA P900059	Letter Holli I DA	meeting
PMA P900059	Letter from FDA	Approval of Protocol 13391
l .	Letter Holli PDA	Approval of Protocol 13391
Amendment 11	Submission to FDA	Program Paner
PMA P900059	Telephone Call with FDA	Progress Report Discussion regarding panel meeting
1 WA 1 300033	Telephone Call With FDA	Discussion regarding panel meeting
PMA POOOES		Asknowledgement of receipt of E/11/02 December
l .	Telephone Call with EDA	Acknowledgement of receipt of 5/11/92 Progress
 	relephone Call With FDA	Report and discussion regarding panel meeting
1	Tolophone Cell with EDA	Request for update regarding panel meeting and
Vinenament 2	relephone Call With FDA	status of PMA
DAMA DOCCOEG	Talanhana Call with FDA	Decree for information and the
 	Telephone Call With FDA	Request for information regarding panel meeting
	Subminsion to FDA	Danasa Bassa A
Supplement 46	Submission to FUA	Progress Report
DNAA DOOOOEO	Talanhana Call wish FDA	Decree for inferred at the second
	relephone Call With FDA	Request for information regarding panel meeting
	504	
Amenament 3	Letter to FDA	Request for information regarding panel meeting
D144 D000050	D 144	
	Panel Meeting	Review of PMA by Radiologic Device Advisory Panel
· · · · · · · · · · · · · · · · · · ·	FAX to FDA	Request for minutes from 7/14/92 panel meeting
	Submission to FDA	Transmittal of tapes from 7/14/94 panel meeting
1		
	Submission to FDA	Response to 3/31/92 letter from FDA
Supplement 49	Submission to FDA	Information regarding manufacturing process
		Acknowledgement of receipt of 7/2/92 Progress
		Report
PMA P900059	Telephone Call with FDA	Request for status of PMA
	·	
PMA P900059	Telephone Call with FDA	Discussion regarding product labeling requirements
PMA P900059		Request for status of PMA
PMA P900059	Telephone Call with FDA	Request for status of PMA
IDE G870144		Acknowledgement of receipt of 8/5/92 submission to
Supplement 49	Letter from FDA	FDA
PMA P900059	Telephone Call with FDA	Request for status of PMA
		Request for status of PMA and discussion of post-
PMA P900059	Telephone Call with FDA	market approval clinical studies
IDE G920008		Request for additional information regarding Protocol
Amendment 2	Letter from FDA	13491
PMA P900059	Telephone Call with FDA	Discussion regarding technical references
	•	
	Telephone Call with FDA	Discussion regarding 9/3/92 letter from FDA
	PMA P900059 PMA P900059 IDE G870144 Supplement 49 PMA P900059 PMA P900059 IDE G920008 Amendment 2	Amendment 11 PMA P900059 Amendment 3 Telephone Call with FDA PMA P900059 Telephone Call with FDA PMA P900059 Telephone Call with FDA PMA P900059 Amendment 3 PMA P900059 Amendment 3 PMA P900059 Amendment 3 PMA P900059 Amendment 3 PMA P900059 Amendment 12 IDE G920008 Amendment 2 IDE G870144 Supplement 49 Submission to FDA IDE G870144 Supplement 49 IDE G870144 Supplement 49 PMA P900059 Telephone Call with FDA

9/17/92	PMA P900059	Telephone Call with FDA	Request for status of PMA
	IDE G920008		Additional discussion regarding 9/3/92 letter from
9/18/92	Amendment 2	Telephone Call with FDA	FDA
	IDE G920008		
9/21/92	Amendment 3	Submission to FDA	Response to 9/3/92 letter from FDA
	IDE G920008	1	
9/23/92	Amendment 3	Telephone Call with FDA	Discussion regarding Protocol 13491
			Request for informal review of post-market approval
9/29/92	PMA P900059	FAX to FDA	clinical studies
9/29/92	PMA P900059	Telephone Call with FDA	Request for status of PMA
9/30/92	PMA P900059	Telephone Call with FDA	Confirmation of 10/2/92 meeting at FDA
	PMA P900059 IDE		
	G920008		Discussion regarding post-market approval clinical
10/2/92	Amendment 3	Meeting at FDA	studies and Protocol 13491
10/4/92	PMA P900059	Telephone Call with FDA	Request for status of PMA
10/5/92	PMA P900059	Telephone Call with FDA	Request for status of PMA
	IDE G920187		
10/12/92	Original	Submission to FDA	Addition of Protocol 13192
10/16/92	PMA P900059	Letter to FDA	Draft post-market approval clinical study protocol
10/16/92	IDE G920187	Letter from FDA	Acknowledgment of receipt of Protocol 13192
			Request for informal review of draft post-market
			approval clinical study protocol as submitted on
10/22/92	PMA P900059	Letter to FDA	10/16/92
10/22/92	IDE G920008	Letter from FDA	Approval of Protocol 13491
	PMA P900059		
10/26/92	Amendment 13	Submission to FDA	Progress Report
10/30/92	PMA P900059	Telephone Call with FDA	Request for status of PMA
	IDE G920008		
11/3/92	Supplement 1	Submission to FDA	Request for additional study site for Protocol 13491
11/9/92	PMA P900059	Telephone Call with FDA	Request for status of PMA
11/10/92	PMA P900059	Telephone Call with FDA	Request for status of PMA
11/10/92	PMA P900059	Telephone Call with FDA	Discussion regarding export to Japan
			Confirmation that 11/3/92 submission to FDA was
			correctly logged in as Supplement 1 and not
11/10/92	IDE G920008	Telephone Call with FDA	Amendment 4
11/10/92	PMA P900059	Telephone Call with FDA	Request for status of PMA
	IDE G870144		
11/10/92	Supplement 50	Submission to FDA	Request for changes to Protocol 13291
			Request for additional information regarding Protocol
11/11/92	IDE G920187	Letter from FDA	13192
			Request for additional information regarding Protocol
11/12/92	IDE G920008	Letter from FDA	13491
	PMA P900059		
11/13/92	IDE G920187	Telephone Call with FDA	Request for status of PMA and Protocol 13192
11/17/92	PMA P900059	Telephone Call with FDA	Request for status of PMA
11/17/92	IDE G920187	Telephone Call with FDA	Discussion regarding 11/12/92 letter from FDA
11/18/92	PMA P900058	Letter from FDA	Request for additional information
11/18/92	PMA P900059	Telephone Call with FDA	Request for meeting at FDA
11/10/32	II MV I 90009	Treseptione Call With FDA	Inednest in ineering at LDV

	PMA P900059	<u> </u>	
11/19/92	IDE G920187	FAX to FDA	Agenda for upcoming meeting at FDA
	PMA P900059		Discussion regarding status of PMA and Protocol
11/23/92	IDE G920187	Meeting with FDA	13192
,	PMA P900059 IDE		
11/24/92	G920187	Letter to FDA	Minutes from 11/23/92 meeting with FDA
11/25/92	PMA P900059	Telephone Call with FDA	Discussion regarding 11/18/92 letter from FDA
	IDE G920008		
12/3/92	Supplement 1	Submission to FDA	Request to add clinical site to Protocol 13491
			Discussion regarding post-market approval clinical
12/4/92	PMA P900059	Telephone Call with FDA	studies and request for meeting at FDA
			Discussion regarding post-market approval clinical
12/7/92	PMA P900059	Telephone Call with FDA	study protocols
	IDE G920008		
12/7/92	Supplement 1	Letter from FDA	Approval of additional clinical site for Protocol 13491
	IDE G870144		
12/11/92	Supplement 50	Letter from FDA	Approval of Protocol 13291 as amended 11/10/92
12/15/92	PMA P900059	Telephone Call with FDA	Discussion regarding manufacturing process
	PMA P900059		
12/30/92	Amendment 14	Submission to FDA	Response to 11/18/92 letter from FDA
			Response to 11/11/92 letter from FDA and request
·	IDE G920187		for change to packaging specifications (Note: only
1/6/93	Amendment 1	Submission to FDA	logged in by FDA for IDE G920187)
	PMA P900059		
1/16/93	Amendment 14	Telephone Call from FDA	Discussion regarding 12/30/93 submission to FDA
1/22/93	PMA and All IDE's	Telephone Call with FDA	Discussion regarding packaging information
1/27/93	PMA P900059	Telephone Call with FDA	Discussion regarding export to Japan
	IDE G870144		
	Supplement 51		
	IDE G920008		
	Supplement 2 IDE		
	G920187		
1/28/93	Supplement 1	Submission to FDA	Follow-up to 1/22/93 telephone call with FDA
			Discussion regarding change to packaging
			specifications as requested in 1/6/92 submission to
1/29/93	PMA and All IDE's	Telephone Call with FDA	FDA
	1		Conditional approval of protocol 13192 and request
			for additional information, and approval of change to
			packaging specifications as requested in 1/6/93
2/5/93	PMA and All IDE's	Letter from FDA	submission to FDA
	-		Discussion regarding post-market approval clinical
2/11/93	PMA P900059	Telephone Call with FDA	study protocols
	IDE G870144		
	Supplement 52		
	IDE G920008		
	Supplement 3 IDE		
	G920187		Progress Report and proposed change to
	Supplement 5	•	

	IDE G920187		
2/22/93	Amendment 1	Telephone Call with FDA	Discussion regarding 2/5/93 letter from FDA
2/22/00		Tolophone Call With TEA	Follow-up to 1/28/93 submission to FDA and request
2/25/93	PMA and All IDE's	Letter from FDA	for additional information
		Lotto: Hom (D/)	Discussion regarding 1/28/93 submission from FDA
3/3/93	PMA and All IDE's	Telephone Call with FDA	and 2/25/93 letter from FDA
0,0,00		Total	Discussion regarding post-market approval clinical
3/5/93	PMA and All IDE's	Telephone Call with FDA	studies and 2/12/93 submission to FDA
			Request for meeting with FDA to discuss post-market
3/9/93	PMA P900059	Telephone Call with FDA	approval clinical studies
3/10/93	PMA P900059	FAX to FDA	Agenda for upcoming meeting at FDA
	IDE G920187		Request for extension of time to respond to 2/5/93
3/10/93	Supplement 2	Submission to FDA	letter from FDA
			Request for status regarding 2/12/93 submission to
3/18/93	PMA and All IDE's	Telephone Call with FDA	FDA
			Conditional approval of proposed change to
			specifications for product usage as requested in
			2/12/93 submission to FDA and request for additional
3/18/93	PMA and All IDE's	Letter from FDA	information
			Revised list of attendees for upcoming meeting with
3/26/93	PMA P900059	FAX to FDA	FDA
		-	
			Discussion regarding 2/12/93 submission to FDA and
3/29/93	PMA and All IDE's	Meeting with FDA	post-market approval clinical study protocols
			Discussion regarding post-market approval clinical
			study protocols and follow-up to 3/29/93 meeting
4/7/93	PMA P900059	Telephone Call with FDA	with FDA
	IDE G920187		Approval of request for extension of time to respond
4/15/93	Supplement 2	Letter from FDA	to 2/5/93 letter from FDA
			Discussion regarding post-market approval clinical
4/15/93	PMA and All IDE's	Telephone Call with FDA	studies and 2/5/93 letter from FDA
•	· .		Discussion regarding post-market approval clinical
4/16/93	PMA P900059	Telephone Call with FDA	study protocols
			Discussion regarding Summary of Safety and
4/16/93	PMA P900059	Telephone Call with FDA	Effectiveness
			Discussion regarding post-market approval clinical
4/21/93	PMA P900059	Telephone Call with FDA	study protocol
	IDE G870144		
	Supplement 53		
	IDE G920187		
	Supplement 6 IDE		
	G920008		
4/26/93	Supplement 4	Submission to FDA	Response to 2/25/93 letter from FDA
			Summary of Safety and Effectiveness, information
			regarding post-market approval clinical study
	PMA P900059		protocols and further response to 2/25/93 letter from
4/28/93	Amendment 15	Submission to FDA	FDA
	PMA P900059		
5/4/93	Amendment 16	Submission to FDA	Progress Report

	PMA P900059 IDE		Discussion regarding Protocol 13192 and request for
5/10/93	G920187	Telephone Call with FDA	status of PMA
<u> </u>	PMA P900059	voiopinone dun voice i bit	Request for confirmation of receipt of 4/28/93 and
5/17/93	Amendment 15 & 16	Telephone Call with FDA	5/4/93 submissions to FDA
***************************************	IDE G870144		Of the scotting to the
5/19/93	Supplement 54	Submission to FDA	Amendment to protocol 13391
	IDE G920187		Response to 2/5/93 letter from FDA regarding
5/21/93	Supplement 3	Submission to FDA	Protocol 13192
	IDE G930102	· .	
5/26/93	Original	Submission to FDA	Addition of Protocol A-1000
			Conditional approval of change to specifications for
			product usage as requested in 2/12/93 submission to
5/27/93	PMA and All IDE's	Letter from FDA	FDA and request for additional information
5/28/93	PMA P900059	Telephone Call with FDA	Request for status of PMA
			Conditional approval of Protocol 13192 and request
6/2/93	IDE G920187	Letter from FDA	for additional information
			Acknowledgment of receipt of Protocol A-1000 and
6/8/93	IDE G930102	Letter from FDA	assignment of IDE number
6/8/93	PMA P900059	Telephone Call with FDA	Request for status of PMA
6/14/93	PMA P900059	Telephone Call with FDA	Request for status of PMA
	IDE G920008		
	Supplement 5 IDE G930102		
	Supplement 1 IDE G870144		
	Supplement 55		Additional information regarding change to
	IDE G920187		specification for product usage as request in 5/27/93
6/16/93	Supplement 7	Submission to FDA	letter from FDA
6/17/93	PMA P900059	Telephone Call with FDA	Request for status of PMA
	•		
	IDE G870144		Conditional approval of Protocol 13391as amended
6/18/93	Supplement 54	Letter from FDA	5/19/93 and request for additional information
6/23/93	IDE G920187	Letter from FDA	Approval of Protocol 13192 as amended 1/6/93
6/25/93	PMA P900059	Telephone Call with FDA	Request for status of PMA
		•	Conditional approval of Protocol A-1000 and request
6/25/93	IDE G930102	Letter from FDA	for additional information
6/28/93	IDE G870144	Letter to FDA	Request for permit to export to Canada
,	IDE G920187		
7/2/93	Supplement 4	Submission to FDA	Additional information regarding Protocol 13192
7/6/93	PMA P900059	Telephone Call with FDA	Request for Status of PMA
7/8/93	PMA P900059	Telephone Call with FDA	Request for status of permit to export to Japan
7/0/02	PMA P900059	Telephone Call with FDA	Request for status of PMA
7/9/93		Tolonhone Call wish CDA	Request for status of Protocol A-1000
7/9/93 7/12/93	IDE G930102	Telephone Call with FDA	1.040001.01.010100.71.1000
	IDE G930102 PMA P900059	Telephone Call with FDA	Request for status of PMA
7/12/93		 	Request for status of PMA
7/12/93		 	

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7/22/02	DNA BOOOGO	Tolombono Coll wish FDA	Daniel Control
7/23/93	PMA P900059	Telephone Call with FDA	Request for status of PMA
7/28/93	PMA P900059	Telephone Call with FDA	Request for status of PMA
7/30/93	IDE G870144	Letter from FDA	Approval of request for permit to export to Canada
8/5/93	PMA P900059	Telephone Call with FDA	Request for status of PMA
0/0/00	IDE G930102	i eleptione Call With FDA	nequest for status of FIMA
8/5/93	Supplement 2	Submission to FDA	Response to 6/25/93 letter from FDA
010133	Supplement 2	Submission to FDA	Acknowledgement of receipt of internal review board
			approval for Protocol 13192 and notification of
			requirement to make change to informed consent
8/5/93	IDE G920187	Letter from FDA	document
8/6/93	PMA P900059	Telephone Call with FDA	Request for status of PMA
	PMA P900059	Telephone Call with FDA	Request for status of PMA
8/10/93	IDE G870144	releptione call with rbA	Second amendment to Protocol 13391 in response to
8/10/93	Supplement 56	Submission to FDA	6/18/93 letter from FDA
8/13/93	PMA P900059	Telephone Call with FDA	
8/16/93		Telephone Call with FDA	Request for status of PMA
	PMA P900059		Request for status of PMA
8/20/93	PMA P900059 PMA and All IDE's	Telephone Call with FDA	Request for status of PMA
8/30/93	 	Telephone Call with FDA	Discussion regarding clinical information
0.40.400	PMA P900059	0 6 22 22 22 22 504	Ned Standard Standard
9/3/93	Amendment 17	Submission to FDA	Notification of legal representative
9/3/93	IDE G930102	Letter from FDA	Approval of Protocol A-1000
9/8/93	PMA P900059	Telephone Call with FDA	Discussion regarding product manufacturing
0.40.00	105 00704 44		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
9/10/93	IDE G870144	Letter from FDA	Approval of Protocol 13391 as amended 8/10/93
	IDE G930102		
9/14/93	Supplement 3	Submission to FDA	Additional information regarding Protocol A-1000
9/15/93	PMA P900059	Telephone Call with FDA	Request for status of PMA
	IDE G870144		
9/20/93	Supplement 57	Submission to FDA	Progress Report
9/22/93	PMA P900059	Telephone Call with FDA	Discussion regarding product specifications
9/23/93	PMA and All IDE's	Letter from FDA	Follow-up to 8/30/93 telephone call with FDA
9/30/93	IDE G870144	Letter to FDA	Request for status of permit to export to Japan
10/4/93	IDE G870144	Letter from FDA	Approval of request for permit to export to Japan
,	IDE G870144		· ·
	Supplement 58	· .	
	IDE G920187		
	Supplement 8 IDE		
	G920008		·
10/11/93	Supplement 6	Submission to FDA	Follow-up to 9/23/93 letter from FDA
	IDE G930102		Acknowledgement of receipt of 9/14/93 submission
10/15/93	Supplement 3	Letter from FDA	to FDA
10/19/93	IDE G870144	Telephone Call with FDA	Discussion regarding export to Canada
			Acknowledgement of receipt of Progress Report dated
10/21/93	IDE G870144	Letter from FDA	9/20/93
	IDE G920187		
10/26/93	Supplement 9	Submission to FDA	Progress Report
11/4/93	PMA P900059	Telephone Call with FDA	Discussion regarding packaging specifications

11/12/93	PMA and All IDE's	Telephone Call with FDA	Discussion regarding clinical information
11/12/00	IDE G870144	Telephone Call With TBA	Discussion regarding chinear information
	Supplement 59	·	
	IDE G920187		
	Supplement 9 IDE		
	G920008		
	1		
	Supplement 7 IDE G930102		
11/12/93	Supplement 4	Submission to FDA	Follow up to 11/12/02 tolophone cell with FDA
11/12/93	IDE G870144	Submission to FDA	Follow-up to 11/12/93 telephone call with FDA
•	Supplement 60		
	IDE G920187		
)	1 .	
	Supplement 10 IDE G920008		
	Supplement 8 IDE G930102		
		Cubariasia a SDA	Hadaa af lawaala aa a Baa
11/18/93	Supplement 5	Submission to FDA	Update of investigator lists
11/10/02	DA4A DOOOOEO	Tologhana Call with FDA	Discussion reporting 44/40/00 as buriaries as FDA
11/19/93	PMA P900059	Telephone Call with FDA	Discussion regarding 11/12/93 submissions to FDA
11/00/00	IDE G930102	Cubariasia as FDA	Additional information was the Durant A 4000
11/22/93	Supplement 6	Submission to FDA	Additional information regarding Protocol A-1000
			Acknowledgement of receipt of Progress Report dated
	IDE 0000407		10/26/93 and request for additional information
11/24/93	IDE G920187	Letter from FDA	regarding Protocol 13192
			Request for status of PMA and discussion regarding
	PMA P900059	Telephone Call with FDA	11/12/93 submissions to FDA
12/6/93	PMA P900059	Fax to FDA	Request to schedule meeting with FDA
			Request for status of PMA and discussion regarding
12/6/93	PMA P900059	Telephone Call with FDA	meeting with FDA
	IDE G920187		
12/6/93	Supplement 12	Submission to FDA	Request to add study site to Protocol 13192
	IDE G920187		:
12/7/93	Supplement 13	Submission to FDA	Correction to 12/6/93 submission to FDA
12/8/93	PMA P900059	Telephone Call with FDA	Request for status of PMA
12/8/93	PMA P900059	Letter from FDA	Request for additional information
	IDE G920187		
12/8/93	Supplement 14	Submission to FDA	Request to add investigator to Protocol 13192
12/12/93	PMA P900059	Telephone Call with FDA	Request for status of PMA
12/14/93	PMA P900059	Fax to FDA	Request for telephone call with FDA
	IDE G870144	· ·	
	Supplement 59	·	
	IDE G920187		
•	Supplement 9 IDE		
	G920008		
	Supplement 7 IDE		
	G930102		Request for additional information regarding 11/12/93
12/16/93	Supplement 4	Letter from FDA	submissions to FDA
	1	1	

			Approval to add study site and investigator as
	IDE G920187		requested in 12/6/93 and 12/8/93 submissions to
12/22/93	Supplements 12 & 14	Letter from FDA	FDA
	IDE G930102		Acknowledgement of receipt of 11/22/93 submission
12/23/93	Supplement 6	Letter from FDA	to FDA
	PMA P900059		
12/24/93	Amendment 18	Submission to FDA	Response to 12/8/93 letter from FDA
1/3/94	PMA P900059	Telephone Call with FDA	Discussion regarding 12/24/93 submission to FDA
1/4/94	PMA P900059	Telephone Call with FDA	Discussion regarding status of PMA
1/5/94	PMA P900059	Fax to FDA	Request for telephone call with FDA to discuss status of PMA
	IDE G920187		
1/6/94	Supplement 15	Submission to FDA	Response to 11/24/93 letter from FDA
	PMA P900059	· .	
1/13/94	Amendment 19	Submission to FDA	Correction to 12/24/93 submission to FDA
1/14/94	PMA P900059	Telephone Call with FDA	Discussion regarding 12/16/93 submission to FDA
1/21/94	PMA P900059	Telephone Call with FDA	Discussion regarding 12/16/93 submission to FDA
	IDE G920008		
1/24/94	Supplement 9	Submission to FDA	Progress Report
	PMA P900059		
1/26/94	Amendment 20	Submission to FDA	Additional response to 12/8/93 letter from FDA
2/2/94	PMA P900059	Telephone Call with FDA	Request for status of PMA
2/3/94	PMA P900059	Fax to FDA	Request for status of PMA
	"		Acknowledgement of receipt of 1/6/94 submission to
2/4/94	IDE G920187	Letter from FDA	FDA.
	IDE G870144		
	Supplement 61 IDE G920187	•	
	Supplement 11		•
•	IDE G920008	·	·
	Supplement 9 IDE		
	G930102		Request for extension of time to respond to 12/16/93
2/4/94	Supplement 6	Submission to FDA	letter from FDA
	IDE G870144		
	Supplement 62		
	IDE G920187		
	Supplement 12		
•	IDE G920008		·
	Supplement 10		·
	IDE G930102		
2/22/94	Supplement 7	Submission to FDA	Response to 12/16/93 letter from FDA
2/24/94	IDE G920008	Letter from FDA	Acknowledgement of receipt of Progress Report dated
3/25/94	PMA P900059	Telephone Call with FDA	Discussion regarding status of PMA
3/25/94	PMA P900059	Fax to FDA	Follow-up to 3/25/93 telephone call with FDA
3/28/94	PMA P900059	Telephone Call from FDA	Request for status of PMA

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			Request for telephone call with FDA to discuss status
3/28/94	PMA P900059	Fax to FDA	of PMA
3/29/94	PMA P900059	Telephone Call with FDA	Discussion regarding status of PMA
3/29/94	PMA P900059	Fax to FDA	Follow-up to 3/25/94, 3/28/94 and 3/29/94 telephone calls with FDA
3/30/94	PMA P900059	Fax to FDA	Additional follow-up to 3/28/94 telephone call with FDA
	IDE G870144		
	Supplement 62 IDE G920187	·	
	Supplement 12		·
	IDE G920008		
	Supplement 10		
	IDE G930102		
3/31/94	Supplement 7	Letter from FDA	Acceptance of 2/22/94 submissions to FDA
<u> </u>	PMA P900059		
4/4/94	Amendment 21	Submission to FDA	Information regarding marketing and clinical studies
	IDE G940051		
4/15/94	Original	Submission to FDA	Addition of protocol A-3000.
4/19/94	IDE G940051	Letter from FDA	Acknowledgement of receipt of Protocol A-3000
			Notification that PMA is approvable and request for
4/26/94	PMA P900059	Letter from FDA	additional information
	PMA P900059		
5/4/94	Amendment 22	Submission to FDA	Response to 4/26/94 letter from FDA
			Request for additional information regarding Protocol
5/18/94	IDE G9400051	Letter from FDA	A-3000
	PMA P900059		
5/31/94	Supplement 22	Telephone Call with FDA	Discussion regarding 5/4/94 submission to FDA
	PMA P900059		
6/1/94	Supplement 22	Telephone Call from FDA	Discussion regarding 5/4/94 submission to FDA
	PMA P900059		Follow-up to 5/31/94 and 6/1/94 telephone calls with
6/2/94	Supplement 22	Fax to FDA	FDA
	PMA P900059		Additional follow-up to 5/31/94 and 6/1/94 telephone
6/6/94	Amendment 23	Submission to FDA	calls with FDA
	IDE G940051	·	
7/15/94	Amendment 1	Submission to FDA	Response to 5/18/94 letter from FDA
	IDE G870144		
7/20/94	Supplement 63	Submission to FDA	Progress Report
	IDE G920008		
7/20/94	Supplement 12	Submission to FDA	Final Report for Protocol 13491
8/5/94	PMA P900059	Notification from FDA	FDA APPROVAL OF PMA

Attorney Docket 248432800200

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: U.S. Patent 4,844,882

Issued: July 4, 1989

To: Widder et al.

For:

CONCENTRATED STABILIZED

MICROBUBBLE-TYPE ULTRASONIC

IMAGING AGENT

DECLARATION

The Honorable Commissioner of Patents and Trademarks Box Patent Extension Washington, D.C. 20231

Sir:

The undersigned, attorney for Molecular Biosystems, Inc. in connection with the application for patent term extension, which is the Applicant for Extension of Patent Term under 35 USC §156 with regard to U.S. Patent No. 4,844,882, hereby declares that:

- 1. I am an attorney authorized to practice before the United States Patent and Trademark Office and have general authority to act on behalf of the owner in connection with the application for patent term extension of U.S. Patent No. 4,844,882.
- 2. I have reviewed and understand the contents of the application being submitted pursuant to 35 USC §156 and 37 CFR §1.740.
 - 3. I believe the patent is subject to extension pursuant to 35 USC §156 and 37 CFR §1.710;
- 4. I believe an extension of the length claimed is justified under 35 USC §156 and the applicable regulations.
- 5. I believe the patent for which the extension is being sought meets the conditions for extension of the term of a patent as set forth in 37 CFR §1.720.
- 6. I hereby declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any extension of patent term issuing thereon.

September 21, 1994. Date

Freddie K. Park, Reg. No. 35,636

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